

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

| | |
|---|---|
| Date of mailing (day/month/year) 23 April 1999 (23.04.99) | |
| International application No. PCT/US98/15148 | Applicant's or agent's file reference 07265/133WO1 |
| International filing date (day/month/year) 24 July 1998 (24.07.98) | Priority date (day/month/year) 31 July 1997 (31.07.97) |
| Applicant LEE, Se-Jin et al | |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

24 February 1999 (24.02.99)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

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|---|--|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland | Authorized officer Lazar Joseph Panakal |
| Facsimile No.: (41-22) 740.14.35 | Telephone No.: (41-22) 338.83.38 |

PATENT COOPERATION TREATY

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REC'D 23 NOV 1999

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

| | | |
|--|--|---|
| Applicant's or agent's file reference 07265/133W01 | FOR FURTHER ACTION | See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |
| International application No. PCT/US98/15148 | International filing date (day/month/year) 24 JULY 1998 | Priority date (day/month/year) 31 JULY 1997 |
| International Patent Classification (IPC) or national classification and IPC Please See Supplemental Sheet. | | |
| Applicant THE JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE | | |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

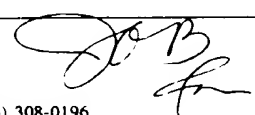
2. This REPORT consists of a total of 6 sheets

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of report with regard to novelty, inventive step or industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

| | |
|--|---|
| Date of submission of the demand 24 FEBRUARY 1999 | Date of completion of this report 04 NOVEMBER 1999 |
| Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 | Authorized officer  PREMA MERTZ |
| Facsimile No. (703) 305-3230 | Telephone No. (703) 308-0196 |

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/15148

I. Basis of the report

1. This report has been drawn on the basis of (Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments):

☒ the international application as originally filed.

☒ the description, pages 1-27, as originally filed.

pages NONE, filed with the demand.

pages NONE, filed with the letter of

pages, filed with the letter of

☒ the claims, Nos. 1-42, as originally filed.

Nos. NONE, as amended under Article 19.

Nos. NONE, filed with the demand.

Nos. NONE, filed with the letter of

Nos., filed with the letter of

☒ the drawings, sheets/fig. 1, as originally filed.

sheets/fig. NONE, filed with the demand.

sheets/fig. NONE, filed with the letter of

sheets/fig., filed with the letter of

2. The amendments have resulted in the cancellation of:

☒ the description, pages NONE.

☒ the claims, Nos. NONE.

☒ the drawings, sheets/fig. NONE.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of

☐ the entire international application.

☒ claims Nos. 12-42

because:

☐ the said international application, or the said claim Nos. _ relate to the following subject matter which does not require international preliminary examination (*specify*).

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _ are so unclear that no meaningful opinion could be formed (*specify*).

☐ the claims, or said claims Nos. _ are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for said claims Nos. 12-42.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/15148

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**1. STATEMENT**

Novelty (N)

Claims 1-11 YESClaims NONE NO

Inventive Step (IS)

Claims 1-11 YESClaims NONE NO

Industrial Applicability (IA)

Claims 1-11 YESClaims NONE NO**2. CITATIONS AND EXPLANATIONS**

Claims 1-11 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest growth differentiation factor-16 (GDF-16), a polynucleotide encoding GDF-16, a vector and a host cell.

----- NEW CITATIONS -----

NONE

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

The description is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 5 because it fails to adequately enable practice of the claimed invention because:
the description is not enabling for "all GDF-16" as recited in claim 1, because the description only enables a GDF-16 of amino acid sequence shown in Figure 1, the polypeptide having specific characteristics. The term "GDF-16" encompasses amino acid sequences that can deviate from the amino acid sequence shown in Figure 1, therefore, different proteins with different amino acid sequences but the activity of GDF-16 would be encompassed by the claims. Specifically, the instant description does not identify those amino acid residues in the amino acid sequence of GDF-16 which are essential for its biological activity and structural integrity and those residues which are either expendable or substitutable. In the absence of this information a practitioner would have to resort to a substantial amount of undue experimentation in the form of insertional, deletional and substitutional mutation analysis of over 100 amino acid residues before they could even begin to rationally design a functional GDF-16 polypeptide having other than a natural amino acid sequence. The disclosure of a single natural amino acid sequence is clearly insufficient support for claims which encompass any and all GDF-16 polypeptides, including mutants thereof.

Claims 1-2, 4-11 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph.

Claim 3 is objected to under PCT Rule 66.2(a)(v) as lacking clarity under PCT Article 6 because the claim is indefinite for the following reason:

Claim 3 recites "hybridize", which is a conditional limitation because a polynucleotide which could hybridize under conditions of low stringency to DNA encoding the GDF-16 polypeptide of Figure 1, might fail to hybridize under conditions of high stringency.

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.

PCT/US98/15148

Supplemental Box

(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

Sheet 10

CLASSIFICATION:

The International Patent Classification (IPC) and/or the National classification are as listed below:

IPC(6): C12N 15/12, 15/16, 15/18, 15/63, 15/64, 15/66; C07K 14/46, 14/47, 14/475 and US Cl.: 530/350; 435/69.1, 71.1, 71.2, 325, 471, 252.3, 320.1

PCTWORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

| | | | |
|--|--|-----------|---|
| (51) International Patent Classification ⁶ : C12N 15/12, 15/16, 15/18, 15/63, 15/64, 15/66, C07K 14/46, 14/47, 14/475 | | A1 | (11) International Publication Number: WO 99/06556 (43) International Publication Date: 11 February 1999 (11.02.99) |
| (21) International Application Number: PCT/US98/15148 (22) International Filing Date: 24 July 1998 (24.07.98) (30) Priority Data: 60/054,606 31 July 1997 (31.07.97) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application US 60/054,606 (CON) Filed on 31 July 1997 (31.07.97) (71) Applicant (for all designated States except US): THE JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE [US/US]; 720 Rutland Avenue, Baltimore, MD 21205 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): LEE, Se-Jin [US/US]; 6711 Chokeberry Road, Baltimore, MD 21209 (US). HUYNH, Thanh, V. [US/US]; 5510 South Bend Road, Baltimore, MD 21209 (US). SEBALD, Suzanne [US/US]; 1836 Montevideo Road, Jessup, MD 20794 (US). (74) Agent: HAILE, Lisa, A.; Fish & Richardson P.C., Suite 1400, 4225 Executive Square, La Jolla, CA 92037 (US). | | | (81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> |
| (54) Title: GROWTH DIFFERENTIATION FACTOR-16 (57) Abstract <p>Growth differentiation factor-16 (GDF-16) is disclosed along with its polynucleotide sequence and amino acid sequence. Also disclosed are diagnostic and therapeutic methods of using the GDF-16 polypeptide and polynucleotide sequences.</p> | | | |

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| DK | Denmark | LK | Sri Lanka | SE | Sweden | | |
| EE | Estonia | LR | Liberia | SG | Singapore | | |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/15148

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : Please See Extra Sheet.

US CL : 530/350; 435/69.1, 71.1, 71.2, 325, 471, 252.3, 320.1

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/350; 435/69.1, 71.1, 71.2, 325, 471, 252.3, 320.1

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
NONEElectronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Please See Extra Sheet.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| A | WO 94/15949 A1 (JOHNS HOPKINS UNIVERSITY SCHOOL OF MEDICINE) 21 July 1994 (21/07/94), see entire document. | 1-11 |
| A | WO 86/06076 A1 (BIOTECHNOLOGY AUSTRALIA PTY. LTD.) 23 October 1986 (23/10/86), see entire document. | 1-11 |



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

B earlier document published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T

later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X

document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y

document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

Z

document member of the same patent family

Date of the actual completion of the international search

14 OCTOBER 1998

Date of mailing of the international search report

29 OCT 1998

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231

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Authorized officer

PREMA MERTZ

Telephone No. (703) 308-0196

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US98/15148

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

1-11

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US98/15148A. CLASSIFICATION OF SUBJECT MATTER:
IPC (6):

C12N 15/12, 15/16, 15/18, 15/63, 15/64, 15/66; C07K 14/46, 14/47, 14/475

B. FIELDS SEARCHED

Electronic data bases consulted (Name of data base and where practicable terms used):

APS, CAS ONLINE, MEDLINE, BIOSIS, EMBASE, CAPLUS

search terms: growth differentiation factor-16, GDF-16, DNA, polynucleotide, nucleic acid, polypeptide, protein, recombinant, cloning.

BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claims 1-11, drawn to growth differentiation factor-16 (GDF-16), a polynucleotide encoding GDF-16, a vector and a host cell.

Group II, claims 12-14, drawn to antibodies that bind GDF-16.

Group III, claims 15-21, drawn to a method of detecting a cell proliferative disorder in a specimen using antibodies that bind GDF-16.

Group IV, claims 22-23, 25-41, drawn to a method of treating a cell proliferative disorder with antibodies that bind GDF-16.

Group V, claims 22, 24-38, drawn to a method of treating a cell proliferative disorder with a GDF-16 antisense sequence.

Group VI, claim 42, drawn to a method for identifying a GDF-16 receptor polypeptide using a cell expressing a GDF-16 receptor or a soluble receptor.

The inventions listed as Groups I-VI do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The inventions listed as Groups I-VI do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Pursuant to 37 C.F.R. § 1.475 (d), the ISA/US considers that where multiple products and processes are claimed, the main invention shall consist of the first invention of the category first mentioned in the claims and the first recited invention of each of the other categories related thereto. Accordingly, the main invention (Group I) comprises the first-recited product, GDF-16, a polynucleotide encoding GDF-16, a vector and a host cell. Further pursuant to 37 C.F.R. § 1.475 (d), the ISA/US considers that any feature which the subsequently recited products and methods share with the main invention does not constitute a special technical feature within the meaning of PCT Rule 13.2 and that each of such products and methods accordingly defines a separate invention.